Steps to Get an Approval of a New Animal Drug Application (NADA)

...and how INADs fit into the scheme

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Presented by:
Jim Bowker
UISFWS, AADAP Program
Bozeman, MT

In a nutshell….

- **Sponsor needs to demonstrate to CVM that the product is:**
  - **Effective (works as advertised)**
  - **Safe**
    - **Fish**
    - **Humans**
    - **Environment**
  - **Can be manufactured consistently**

Challenge

- **Human and Major animal drugs:**
  - **One drug** (e.g., penicillin)
  - **One species** (e.g., “all men are created equal,” a cow is a cow)
  - **One disease claim** (e.g., strep throat)

- **Fish:**
  - **One drug** (e.g., Chloramine-T)
  - **Many fish species** (e.g., rainbow trout, walleye, catfish, etc, etc….since a fish is not a fish is not a fish)
  - **Many disease claims** (e.g., BGD, external columnaris, external flavobacteriosis, etc, etc)

Other Challenges

- **Economic incentives are practically NIL!**
  - Help from public sector critical
- **People eat fish**
  - Drug residues safe and at safe levels in fish tissue
- **Hatchery effluent discharges into environment (directly into surface water)**
  - Concern from public and NGO's
- **Potential widespread distribution of hatchery effluent discharge**
  - Antimicrobial resistance

Components of a NADA Submission

- Effectiveness
- Safety to the target species
- Human food safety (in food producing animals)
- Labeling
- Environmental assessment
- Chemistry, manufacturing, and controls
- Freedom of Information Summary
- All Other Information

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Chemistry, Manufacturing, and Control

- Demonstrate that what you developed in the lab can be made in bulk
  - Identity
  - Strength
  - Quality
  - Purity
  - Potency
  - Consistency from batch to batch

Human Food Safety

- Short and long term toxicology studies
- Total residue and metabolism studies*
- Analytical method validation studies*
- Total residue depletion studies*

* Used to establish withdrawal period

Environmental Assessment

- Goal is to conduct EA to support a “finding of no significant impact” (FONSI)
- May include information on the introduction of the drug into the environment through:
  - Manufacturing
  - Use
  - Disposal
- Fate of drug in the environment
- Effect of drug on the environment

Target Animal Safety

- Demonstrate safety of highest proposed drug dosage to the target species when animals are:
  - Overdosed
  - Overexposed
- Monitor/evaluate
  - Mortality
  - Histopathologies
  - Behavior

Efficacy

- **Demonstrate effectiveness at the lowest proposed dosage through:**
  - **Pivotal studies (Lab or field studies) – only need a few**
    - **Provide high quality, scientifically valid, statistically defensible data**
    - **Follow a detailed and CVM-accepted research study protocol**
  - **INAD studies – need data collected under production conditions, on numerous fish species, under a variety of environmental conditions!**
    - **Supportive or ancillary data**
    - **Follow a CVM-accepted use protocol**

Pivotal Efficacy Studies

- **Not necessarily difficult…but always rigorous…and often challenging**
  - Natural disease outbreak, detailed pathogen report
  - Production-like conditions
  - Dose verification
  - Blinding, randomized, replication, non-treated controls, etc.
  - Data quality control
  - BIG Final Study Report

INAD Efficacy Studies

- **Data collected during treatment of production fish**
  - **Required:**
    - Mortality (or other) and water quality data
    - Adverse effects/toxicity
    - Adherence to withdrawal period
  - **Not required**
    - Controls
    - Replication
    - Pathology report
    - Dose verification
    - BIG REPORT

How INAD data fits into the NADA Technical Section

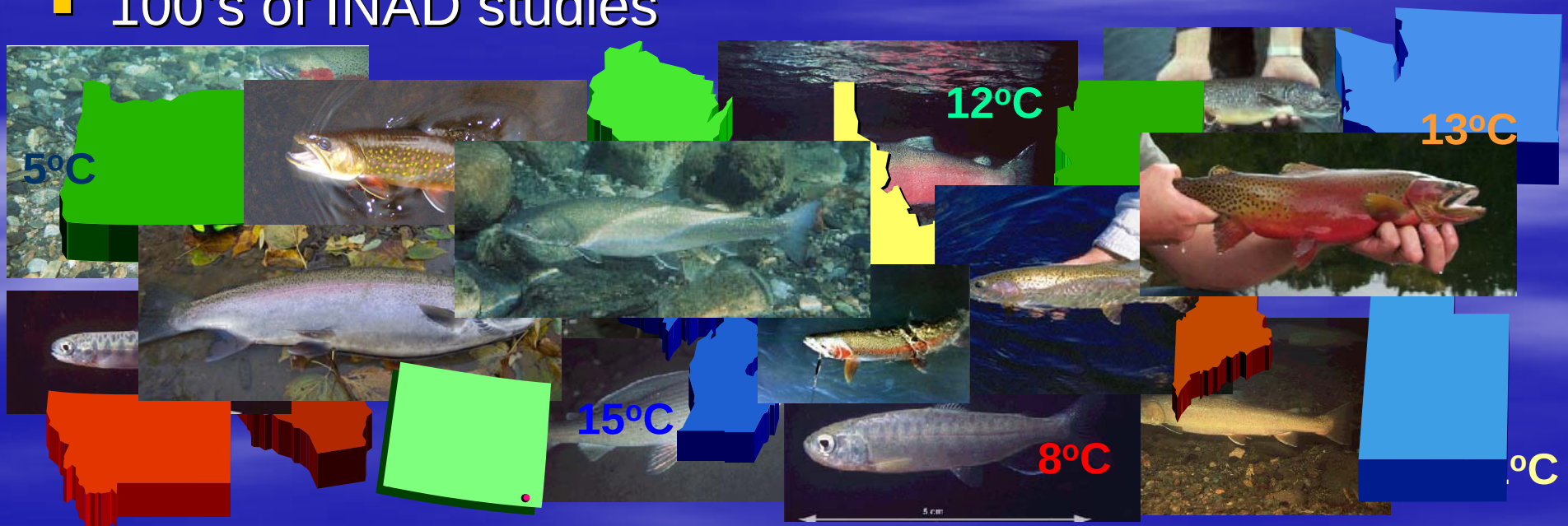
- **Need data from a minimum of 2 – 3 pivotal studies**
  - On representative fish species for each fish group (cold-, cool-, or warmwater fish) for each disease claim
- **Need data from lots of INAD studies**
  - For same fish species under different environmental conditions from other parts of the country
  - On a variety fish species within each fish group under a variety of rearing conditions

For Example:

Chloramine-T

- Three pivotal studies
  - Rainbow trout (Hotchkiss NFH - CO)
  - Apache trout (Williams Creek NFH - AZ)
  - Chum salmon (Quilcene NFH - WA)

- 100's of INAD studies



How you can help

- **Participate in AADAP's NIP (or other INAD program)**
  - Use INADs as described in the Use Protocol
  - Fill out forms completely, write legibly, sign and date forms
  - Generate as much useful data as possible
  - Describe whether treatment worked or not…and if not, why
- **Be patient….we're getting there…slowly**

Questions?